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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/065,330	04/23/98	WALKER	A 2500.097US2

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EXAMINER

ART UNIT	PAPER NUMBER
1647	25

DATE MAILED:

09/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/065,330

Applicant(s)

WALKER

Examiner
Christine Saoud

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 9-11 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 9-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

- ☐ Certified copies of the priority documents have been received.
- ☐ Certified copies of the priority documents have been received in Application No. _____
- ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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SUPPLEMENTAL OFFICE ACTION

In response to Applicant's phone call of July 27, 2001, it became apparent that the Office action of 09 July 2001 was incomplete in that it failed to address the arguments presented in paper #17 (and requested entry in paper #23).

Therefore, a Supplemental Office Action appears below. Applicant's time for response begins at the mailing of the instant Office action.

Status of claims

1. Claims 14-16 were canceled as requested in the amendment of paper #17, filed 05 March 2001. Claims 1-6 and 9-11 are pending in the instant application.

Claim Rejections - 35 USC § 103

2. Claims 1-6 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Cooke et al. (U.S. Pat. No. 4,725,549) and A. M. Walker (TEM, 5(5): 195-200) in view of Maciejewski et al. (J. Biol. Chem. 270(17): 27661-27665, 1995, for the reasons of record in paper #13 and 16.

Applicant argues at page 2 of the response (paper #17) that Walker fails to teach that "modified recombinant non-phosphorylated prolactin acts to antagonize the growth-promoting effects of non-phosphorylated prolactin". It would appear that Applicant intended to say that the recombinant "phosphorylated prolactin antagonizes the effects of non-phosphorylated prolactin.

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Applicant is correct that Walker does not anticipate the instant invention, but it is the combined teachings of Cooke, Walker and Maciejewski that make the instant invention obvious. With regard to Walker, as stated previously in paper #16, Walker teaches at page 197 that "phosphorylated PRL clearly acts as a superantagonist, with approximately one-tenth the concentration of phosphorylated Prl neutralizing the growth-promoting effects of the rest of the PRL". Maciejewski teach that substituted prolactin mimics phosphorylation, therefore, one of ordinary skill in the art would reasonably expect that a substituted prolactin, which mimics phosphorylation, would possess the antagonistic activity as taught by Walker. Applicant again argues that Maciejewski does not teach antagonism. As pointed out previously, the fact that the molecule of Maciejewski did not stimulate cell proliferation in the Nb2 rat lymphoma bioassay says nothing positive or negative with regard to antagonistic activity, contrary to Applicant's arguments.

Applicant argues that Maciejewski do not provide any data demonstrating that S90E prolactin acts like phosphorylated prolactin. This argument is not persuasive because Maciejewski specifically state that the based on UV absorbances and biological activities measured in the NB2 rat lymphoma assay (ED50 values), the S90E prolactin mimics the wild-type phosphorylated prolactin (see abstract). It is noted that Maciejewski did not perform an experiment to determine whether the mutated protein was an antagonist, but the reference clearly compared the two molecules and the conclusion of mimicry was based on scientific data. The reference clearly states "[replacement of serine 90 in bPRL with glutamic acid produced a

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hormone that behaved similarly in the Nb2 biological assay to the biological isolate of phosphorylated bPRL. The results confirm our interpretation of previous sequence and stoichiometry studies (20) that demonstrated that serine 90 to be the most frequently phosphorylated and probably responsible for the reduced biological activity of the phosphorylated hormone." (See Maciejewski at page 27664, column 1 under "Discussion".)

Applicant argues at page 5 of the response that Maciejewski indicates that phosphorylated bPRL does not compete with non-phosphorylated bPRL for binding to the PRL receptor in Nb2 cells, and that this statement teaches away from an antagonistic molecule. This argument is not persuasive because according to Walker, the phosphorylated protein does indeed act as an antagonist in at least two target tissues as evidenced by the passages cited by Applicant.

Applicant asserts that the statement of Walker that "[w]hether this superantagonism is achieved by a much increased affinity for the receptor or initiation of a different signal cascade within the cell is unknown at present" does not teach that antagonism could be achieved by other than binding to the receptor. This argument is not persuasive because the passage does not state that "initiation of a different signal cascade within the cell" is upon receptor binding, and one cannot read such a conclusion into the recited statement without more evidence that this was the true

nature of the statement. Additionally, Walker indicates "we know that monophosphorylated PRL is an antagonist to non-phosphorylated prolactin" (see page 197, column 3). Therefore, the combination of references clearly suggest that the substituted prolactin mimics phosphorylation, and that phosphorylation results in an antagonistic molecule, therefore, one of ordinary skill in the

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art would reasonably conclude that substitution to mimic phosphorylation would likely generate an antagonistic molecule, absent evidence to the contrary.

Conclusion

3. No claim is allowed.

4. All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September 13, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud